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U.S. Senate
Committee on Health, Education, Labor and Pensions
Protecting Human Subjects in Research: Are Current Safeguards Adequate?
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Mr. Chairman and members of the committee, my name is David Charles. I am a physician and director of the Movement Disorders Clinic and Neurology Residency Training Program at Vanderbilt University Medical Center. I also serve as chairman of the National Alliance of Medical Researchers and Teaching Physicians, a coalition of doctors, scientists and health care providers dedicated to the advancement of medicine through technology. I am testifying today in my role as chairman of the National Alliance of Medical Researchers and Teaching Physicians.

It is a special privilege for me to comment on the important issue before this committee and I greatly appreciate the opportunity.

As a doctor and an American, I'm gratified that the Public Health Subcommittee includes some of the most distinguished names in the U.S. Senate. I am delighted that this committee includes my fellow Tennessean and clinical researcher, Senator Frist

My comments represent the perspective of someone who works full-time in clinical research and teaching. And I might start by asking the semi-rhetorical question of "what is clinical research?" For our purposes here, let's think of clinical research as the phase of medical science where the discoveries of the laboratory meet the realities of the human body.

No drug, no medical device, no surgical procedure will ever prove its value to cure disease or ease suffering until it has been tested on people. Yet the investigation of new treatments on humans, even if the testing may lead to a cure of a devastating disease, arouses our sensitivities and concerns, as well it should.

We all recognize that safeguarding the health of those who serve as subjects in clinical trials and preserving the integrity of the research process is essential. These are common goals supported by the clinical research community, the general public and, I'm sure, by the members of this committee.

In terms of the issues under consideration by the committee, I might paraphrase the oft-quoted Mr. Churchill and say: "Never have so many disagreed so little about so much."

But I'm also reminded of the cynical summary Calvin Coolidge gave one Sunday afternoon of a sermon he had heard that morning.

"The preacher talked about sin," said Coolidge. "He was against it."

Today, we are all against exposing people involved in clinical trials to excessive risk. We're all opposed to violating the privacy of medical data during the research process. And certainly, we're all concerned about potential conflicts of interest among those who conduct clinical research and the health care companies that sometimes fund such research.

But being opposed to those things is the easy part. Improving the safeguards already in place is much more complicated and difficult.

We have to recognize, for instance, that clinical researchers testing and refining new drugs or medical devices have to work closely with the companies that created those products. Vital medical research couldn't take place without that kind of cooperation.

Can we still conduct clinical research that might involve potential conflicts of interest? We can so long as there are strong safeguards in place that protect the outcome of the research and the well being of the human subjects.

The joint challenge of the medical profession and public policy makers is to strengthen safeguards without creating new regulations so burdensome that they make it impossible to complete vital research. Let's not throw the baby out with the bath water.

And let me emphasize --- my concern about burdensome regulations is not code for eliminating vigorous oversight, by government and by our own profession. Like most doctors, I recognize the need to have others looking over every step of my work during a clinical trial to safeguard against potential conflicts of interest and to protect the health, well being, and privacy of the people participating. That kind of scrutiny comes with the territory in our profession.

But society loses if regulations to protect the public become obstacles to serving the public. That principle applies to the issue of protecting the health of human subjects in clinical trials and to the issue of preventing conflicts of interest in the research community.

When something goes dangerously wrong in a clinical research effort, it gets public attention and feeds the appetite for more regulations. That's understandable. For the sake of perspective, though, let's remember that we are talking about a relative handful of failures against a century's worth of successes.

The abomination of the Tuskegee Syphilis Study still taints public attitudes toward human testing, 30 years after the study was ended. The tragic death of 18-year-old Jesse Gelsinger during a gene transplant study in 1999 left us asking once again, how can we make the process even safer?

Much of the regulations and governing philosophy already in place is effective. All of it is well intentioned. But the system still gives conflicting signals to researchers and the hybrid mix of agencies involved makes it difficult to rationalize those signals. The result can sometimes be research paralysis.

The practical reality is that it can be very, very difficult to navigate the extreme caution and regulatory burden necessary to gain approval to launch a clinical trial. Once the clinical trial is approved, however, it can be even more difficult to actually identify people willing to participate in an investigation and to find the necessary number of people with a particular disease that meet the requirements of the clinical trial. The thicket of reviews required for a clinical trial can be dense to the point of being impenetrable. At times I feel that I need a second career just to handle the paperwork.

As a result, clinical trials simply aren't being done at the rate we all recognize that they should. This is an example of regulations having the right intent but the wrong results. And it's just one example.

So I think this committee could do this nation a great service by simplifying the clinical research regulations and clarifying who has responsibility for enforcing them. I

believe this can be done at the same time you tighten those regulations and promote even more safety and integrity in the research process.

The National Alliance of Medical Researchers and Teaching Physicians would like to commend the federal Department of Health and Human Services and the General Accounting Office for the study they have already made of this issue. The Alliance has also given this our serious attention. As a result, we support the following principles for any new federal legislation.

- **A comprehensive and uniform set of federal protections**
- **Strong, informed, and independent oversight by Institutional Review Boards (IRBs)**
- **Effective privacy protections that do not prevent important archival research**
- **Strong guidelines governing conflicts of interest that require full disclosure of such arrangements**

As a first principle we strongly recommend a comprehensive and uniform set of federal laws assuring that all research is designed and carried out in accord with high ethical standards for protecting human subjects from research risks. As you know, the federal government now relies on what's known as "the Common Rule."

This is a set of requirements endorsed by 17 federal departments and agencies. The Common Rule is the closest thing the federal government has to a comprehensive, uniform set of regulations covering human testing. In practice, however, individual agencies routinely depart from the common rule and make policy on their own, to meet what they see as special circumstances. Today, investigators often face overlapping, confusing, and sometimes contradictory regulatory systems.

The Common Rule's provisions for protecting human subjects from the risks of interventional research should be clarified. Equally important, any proposed legislation should apply to all federally sponsored or regulated research with humans.

The Common Rule badly needs the momentum it would get from being codified into federal law. These statutes should include specific rules for gaining the informed consent of research subjects, and define the circumstances under which waiver of informed consent is justified. However, there are legitimate concerns with codifying the common rule, and we should be careful to ensure that the standards under any legislation be flexible and able to adapt as science continues to evolve.

Any set of rules is only as good as their enforcement. We recommend that the enforcement and interpretation of new codified federal standards for interventional research be handled primarily by strengthened Institutional Review Boards (IRBs).

The new Institutional Review Boards would have clearer authority and more demanding standards for board membership. We recommend that these new boards be overseen by the existing Office of Human Research Protection.

These IRBs would be responsible for reviewing and approving or rejecting all proposed protocols for interventional research.

To protect the independent judgment of these boards, the review fees of the boards could not be paid with equity interest in the company sponsoring the proposed research, or as a share of any royalties arising from the research.

In the important area of protecting the privacy of the medical data of individuals, we support the Secretary of Health and Human Services' March 27, 2002, proposal to modify the federal medical privacy rule. We support a continued effort to improve guidelines for research that analyzes databanks of medical records, health benefit claims and archives of biological materials and genetic information. The goal should be to establish mechanisms that minimize the risk to individuals' privacy while protecting the ability to conduct much needed research.

Consumers are already painfully aware of the vulnerability of their personal data. The perceived lack of data security is the biggest drawback to doing transactions on the Internet. This only reinforces the need to take the initiative in guaranteeing privacy protection for medical data used in research.

And one final but major point addresses the sensitive issue of conflict of interest in the conduct of research.

In the belief that full disclosure is the best form of protection for all concerned, we recommend that prior to evaluation of a research protocol, federal law should require:

- **That the research investigators disclose to the appropriate Institutional Review Board what arrangements have been made for compensation.**
- **That researchers must disclose up-front whether or not they or their immediate families have a proprietary interest in the outcome of the proposed research.**

In this area of avoiding conflicts of interest involving compensation, we also believe it would be beneficial for the IRB to be authorized to consider whether…

A – The arrangements for compensating researchers or their proprietary interests in the research might influence their judgment as to the risk faced by a human subject participating in the research.

And B – Whether the arrangements for compensating human test subjects might unfairly induce some prospective subjects to accept unreasonable risks.

I would just add that clinical researchers share the committee's urgency to reinforce the safety and integrity of clinical research practices. Clinical research was essential to the medical breakthroughs that made the last century the pivotal century in health care and made America's health care the best in the world.

To build on that record in the 21st Century, we need the full confidence of the American public.

Thank you.

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